UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/990,427	11/14/2001	David Botstein	P2730P1C10	4110

35489 7590 03/31/2006

HELLER EHRMAN LLP
275 MIDDLEFIELD ROAD
MENLO PARK, CA 94025-3506

EXAMINER	
CHERNYSHEV, OLGA N	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 03/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/990,427	BOTSTEIN ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *119-123* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *119-123* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Formal matters

1. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1649.

2. Claims 119-123 are under examination in the instant office action.

3. The Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

5. Applicant's arguments filed on February 27, 2006 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections - 35 USC § 101

6. Claims 119-123 stand rejected under 35 U.S.C. 101 because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility for reasons of record fully explained in the previous communications of record. The instant application has provided a description of an antibody to a protein. The instant application does not disclose a specific significance of this antibody to a particular disease, disorder or physiological process, which one would wish to manipulate for a desired clinical effect.

Applicant traverses the rejection on premises that "the Examiner seems to indicate that tumor marker is patentable only of the marker tests positive in a statistically high number of

samples compared to the total number of samples tested or if the tumor tests positive in every tissue type that was studied", and this is not a legally correct standard in determining the utility of the claimed invention (pages 3-4 of the Response). Applicant further refers to *Nelson v. Bowler* case in support of the diagnostic utility of the claimed compounds. Applicant's arguments have been fully considered but are not persuasive for the following reasons.

The data in the instant specification show that gene expression of PRO830 polynucleotide (mRNA) is increased in tumor cell lines and primary tumors. It is noted that out of fourteen lung tumor samples, eleven (79% of cases) did not show an amplification of the PRO830 gene. Based on the information presented, one skilled in the art would reasonably question if the instant disclosed PRO830 nucleic acids could be used as a biological marker for lung cancer. A biomarker by definition is a molecule that is either present/absent or present at altered amount under pathological condition as compared to normal control. In the instant case, since elevation of the gene expression of PRO830 was registered only in 21% of lung cancer cases, it is not clear how PRO830 mRNA could be used as a marker for lung cancer based on their differential expression. Moreover, the instant specification presents no factual evidence or sound scientific reasoning that the instant claimed antibodies, which specifically bind to polypeptides encoded by PRO830 polynucleotides, of which is known that they are overexpressed in 21% cases of lung cancer samples, could have practical utility as cancer markers.

With respect to Applicant's reference to *Nelson v. Bowler*, in that case the Federal Circuit found that the identification of a pharmacological activity of a compound provided an "immediate benefit to the public" and satisfies the utility requirement. However, the fact pattern

in *Nelson* is not analogous to this case; in the instant case Applicant has not provided evidence of pharmacological utility, either *in vivo* or *in vitro*.

At pages 4-9 of the Response, Applicant reviews references brought forward during the prosecution of the instant application and Declarations of Goddard and Polakis. Applicant argues that it is more likely that not that a positive correlation exists between mRNA and protein levels (page 5 and 6) and states that "*Accurate prediction* is not a criteria that is necessary for meeting the utility standard" (middle at page 6) and also that "the utility standard does not require accurate prediction of protein values; only that in a majority of the proteins studies, it is more likely than not that protein levels increased when mRNA levels increased" (middle at page 7). Applicant's arguments have been carefully considered but are not deemed persuasive for reasons that follow.

The full analysis of the publications submitted with the previous replies and also with the Declarations of record was presented in the previous office actions of record. In the instant situation, the nature of the fact sought to be established is whether or not a 2.173 to 2.514-fold amplification of the gene encoding PRO830 in three lung tumors (21%) as compared to a pooled DNA sample from blood is significant in view of the absence of changes in PRO830 expression in eleven samples of lung tumors (79%), and further if these data can be directly extrapolated to the utility of the claimed antibodies that bind PRO830 polypeptides as markers for lung tumors. The Examiner maintains the position that based on the information presented in the instant specification as filed and in Applicant's Responses and Declarations of record, the asserted utility of the claimed antibodies to PRO830 polypeptides is not specific and not substantial. The finding of gene amplification of PRO830 mRNA in three of fourteen analyzed samples of lung

tumors represents at most an interesting finding, a mere invitation to experiment, and clearly not a readily available utility. The PRO830 gene has not been associated with tumor formation or the development of cancer, nor has it been shown to be predictive of such. The instant specification merely demonstrates that the PRO830 genomic DNA may be amplified in some cancers, to minor degree (about 2.5 fold) compared to normal DNA from blood. No mutation or translocation of PRO830 has been associated with any type of cancer *versus* healthy corresponding tissue. It is not know whether PRO830 is amplified in corresponding tissue, and what the relative levels of amplification are. In addition, there is no correlation shown between the increase in gene amplification and amplification of the target protein. In the absence of any of that critical information, all that the specification does is present evidence that the DNA encoding PRO830 may be amplified in a variety of samples and invites the artisan to determine the significance of this increase. The current state of the art clearly evidences that the issue of calculation of protein levels from mRNA values is simply not straightforward predictable. Thus, based on the information presented in the instant specification, one skilled in the art would have to engage in further research and experimentation in order to establish the specific utility of the claimed antibodies.

§101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form *Brenner*, 383, U.S. at 534-35, 148 USPQ at 695. *Brenner's* standard has been interpreted to mean that "vague, general disclosures or arguments of "useful in research" or "useful as building blocks of value to the researcher" would not satisfy §101. See *Kirk*, 376 F. 2d at 945 153 USPQ at 55 (interpreting *Brenner*).

In the instant case, the record does not support Applicant's position that the characterization of a nucleic acid as being amplified in less than 25% cases of lung tumor samples examined, would have suggested a use of the antibodies to the protein encoded by that nucleic acid as tumor markers, or any other basis for patentable utility, to a person skilled in the art at the time the application was filed. In the terms used by the *Brenner* Court, such a characterization does not provide a specific utility in currently available form.

The U.S. Court of Appeals for the Federal Circuit recently addressed the utility requirement in the context of a claim to DNA. *See In re Fisher,* 2005 WL 2139421 (Sept. 7, 2005). The *Fisher* court interpreted *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (1966), as rejecting a "de minimis view of utility" 2005 WL 2139421, at *4. The *Fisher* court held that § 101 requires a utility that is both substantial and specific. *Id.* At *5. The court held that disclosing a substantial utility means "show[ing] that an invention is useful to the public as disclosed in its current form, not that it may be useful at some future date after further research. Simply put, to satisfy the 'substantial' utility requirement, an asserted use must show that the claimed invention has a significant and presently available benefit to the public." *Id.*

The court held that a specific utility is "a use which is not so vague as to be meaningless." *Id.* In other words, "in addition to providing a 'substantial' utility, an asserted use must show that the claimed invention can be used to provide a well-defined and particular benefit to the public." *Id.*

Thus, for reasons fully explained in previous office actions of record and reasons above, the instant rejection is maintained.

Claim Rejections - 35 USC § 112

7. Claims 119-123 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a clear asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Conclusion

8. No claim is allowed.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (571) 272-0870. The examiner can normally be reached on 8:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Olga N. Chernyshev, Ph.D.
Primary Examiner
Art Unit 1649

March 29, 2006